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Filed : January 25, 2001  
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**REMARKS**

Claims 1-7, 9 and 11 are pending in the subject application. Applicants have amended claims 1, 5 and 9 to introduce minor formatting changes. Support for the term "covalently bound" in amended claims 1, 5 and 9 can be found at, *inter alia*, page 10, line 26 to page 11, line 5. Applicants maintain that the amendments to claims 1, 5 and 9 do not introduce any new matter. Accordingly, claims 1-7, 9 and 11 will still be pending and under examination in the subject application upon entry of this Amendment.

Applicants respectfully request that, in view of the remarks made herein, the Examiner withdraw the outstanding rejections.

**Rejections Under 35 U.S.C. §112, First Paragraph**

The Examiner rejected claims 1-7, 9 and 11 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In response, applicants respectfully traverse the Examiner's rejection.

Briefly, claims 1-4 provide a composition of matter comprising Varicella-Zoster Virus 29p protein having an agent covalently bound thereto, wherein the composition enters a mammalian cell upon contact therewith. Claim 5 provides a 29p protein having covalently bound thereto a lipid-soluble moiety which permits

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the 29p protein to be anchored to a lipid membrane. Claims 6 and 7 provide a lipid vesicle comprising the composition of claim 5, wherein the 29p protein facilitates delivery of the vesicle's contents into a mammalian cell. Claims 9 and 11 provide a method of delivering an agent into a mammalian cell, wherein the agent is covalently bound to Varicella-Zoster Virus 29p protein.

The claimed invention is based on applicants' surprising discovery that the Varicella-Zoster Virus 29p protein can readily enter mammalian cells, such as neurons and lymphocytes.

In support of the rejection, the Examiner asserts that the specification and the prior art do not provide a structural/functional basis for one skilled in the art to envision a sufficient number of combinations of 29p variant/bound agent/target cell receptor to describe the claimed genus of such combinations. In essence, the Examiner asserts that neither the specification nor the prior art teach what are "naturally-occurring" variants of the 29p protein and the "agents" attached thereto and that applicants have not provided any working examples of the invention.

In response, applicants maintain that the specification provides written description for the subject matter claimed. First, it is unnecessary that applicants set forth the sequence(s) of naturally occurring 29p protein variants for the written description requirement to be satisfied. Applicants maintain that the 29p protein having SEQ ID NO:2 and capable of entering a cell constitutes a representative number of p29 species for the purpose of written description, given that identifying naturally occurring variants thereof

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would require no undue experimentation.

Applicants further note that, contrary to the Examiner's position, no structure/function relationship need be established for the claimed invention to be adequately described. Indeed, it is sufficient for written description that (i) 29p protein has been shown by applicants to enter mammalian cells and (ii) methods existed in the art for affixing agents to a protein without eliminating the protein's functional properties. Applicants need not teach the specific p29 protein domain(s) responsible for cell entry for this purpose.

In addition, applicants point out that the term "agent" is clearly defined in the specification at, *inter alia*, page 9, lines 22-26, and examples of agents are provided at, *inter alia*, page 9, lines 28-33 and page 10, lines 1-24.

Applicants also point out that the specification need not contain an example of the invention if the invention is otherwise disclosed in such a manner the one skilled in the art will be able to practice it without undue experimentation. Applicants maintain that specification sufficiently describes the invention so that one skilled in the art could make and use the invention without undue experimentation.

In support of the rejection, the Examiner has cited the Berendsen reference for the proposition that "the relationship between the sequence of the protein and its tertiary structure ... is not well understood." Applicants maintain that this reference is inapplicable to the instant invention as it does not mention the 29p protein.

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Finally, applicants stress that in this invention, the p29 protein need not have an affinity for, or naturally bind to, the agent. Rather, in certain embodiments, the protein must simply be "covalently bound" to the agent. This point is made in response to the Examiner's statement that "each claim is drawn towards a potentially broad genus of variants of SEQ ID NO:2 that must retain the ability to bind any agent..." (emphasis added).

Accordingly, applicants maintain that the subject matter of the rejected claims is adequately described in the specification.

The Examiner also rejected claims 1-7, 9 and 11 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In response, applicants respectfully traverse the Examiner's rejection. Applicants' traversal is based, where applicable, on the reasons set forth in response to the Examiner's written description rejection, and on the following reasons.

The test for enablement is whether one skilled in the art could, at the time of the invention, make and use the claimed invention based on the disclosure and information known in the art without undue experimentation. Applicants maintain that the claimed invention satisfies the test for enablement, and that the Examiner has not set forth sufficient grounds for concluding otherwise.

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In support of the rejection, the Examiner asserts that it would require undue experimentation to make and use the claimed invention. Specifically, the Examiner asserts that in view of the factors detailed in In re Wands, (i.e., nature of the invention, breadth of the claims, guidance of the specification, working examples, state of the art, and predictability of the art), undue experimentation would be necessary to practice the invention.

Applicants respectfully disagree with the Examiner's position. First, applicants disagree with the Examiner's characterization of the instant invention as having a "complex" nature. This invention involves delivery of an agent to a mammalian cell via a protein shown by applicants to enter such a cell. Applicants do not see this as a complex invention.

Second, and contrary to the Examiner's position, applicants note that the breadth of the claims is relatively narrow, in that only mammalian cells are recited (as opposed to "any target cell type" as stated by the Examiner). The Examiner's assertions regarding naturally occurring 29p protein variants are addressed above.

Third, applicants maintain that the specification provides adequate guidance for practicing the claimed invention. That is, the experiments in the specification showing 29p entry into mammalian cells, combined with routine methods of covalently affixing agents to proteins and identifying naturally occurring protein variants, would enable one to practice the invention as claimed without undue experimentation. Thus, appropriate guidance is provided by the specification.

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Fourth, as to the state of the art, applicants agree with the Examiner that the concept of using 29p protein to deliver an agent into a target cell is novel. However, applicants also note that, as set forth previously, the concept of using a protein that can readily enter a mammalian cell to deliver an agent to the cell was known in the art.

Applicants therefore maintain that the rejected claims are enabled.

In view of the above remarks, applicants respectfully request that the Examiner withdraw the rejections of claims 1-7, 9 and 11 under 35 U.S.C. §112, first paragraph.

**Rejection Under 35 U.S.C. §112, Second Paragraph**

The Examiner rejected claims 1-7, 9 and 11 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

In support of the rejection, the Examiner asserts that the term "Varicella-Zoster Virus 29p protein" in claims 1-7, 9 and 11 is unclear.

In response, applicants respectfully traverse the Examiner's rejection.

Applicants maintain that the term "Varicella-Zoster Virus 29p protein", as exemplified by SEQ ID NO:2, would be clear to one skilled in the art. Specifically, this protein is defined in the specification as a protein having the sequence in Figure 6

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or a naturally occurring variant thereof. Naturally occurring protein variants, such as polymorphisms, which behave similarly to the protein of Figure 6, can be readily identified, and the meaning of the term "naturally occurring variant" would clearly be understood by one skilled in the art. So long as the metes and bounds of the claims are clear, which they are, it is irrelevant for the purpose of 35 U.S.C. §112, second paragraph, whether the specific sequences of such variants, or the various domains of the protein of Figure 6, are actually set forth in the application.

In view of the above remarks, applicants maintain that amended claims 1-7, 9 and 11 satisfy the requirements of 35 U.S.C. §112, second paragraph.

#### **Conclusion**

Applicants maintain that claims 1-7, 9 and 11 are in condition for allowance, and thus, allowance is respectfully requested.


If a telephone interview would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.



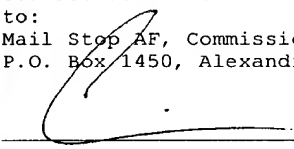
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No fee other than the \$55.00 for the one-month extension of time is deemed necessary with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

  
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